DETAILED ACTION

Response to Arguments

1. The arguments filed on June 24, 2009 have been fully considered. The 35 USC 103 rejection is maintained. Below are responses to Applicant's remarks.

> A skilled medicinal chemist seeking to make new inhibitors of NOS would select a lead compound which is a selective inhibitor of iNOS, the preferred isoform. Beaton *et al.* teaches compounds which are non-selective have undesirable cardiovascular side effects arising from inhibition of the isoform eNOS (see page 1023). Beaton *et al.* further distinguishes the importance of selective NOS inhibitors by disclosing the discovery of one of the most selective inhibitors known, compound **5j**. Compound **5j** is shown to be a potent inhibitor of iNOS with no significant activity toward the undesirable eNOS enzyme (see pages 1023-1024). A skilled artisan seeking to make alternate compounds as inhibitors of nitric oxide synthase would be motivated to select compound **5j** as a lead compound do to its properties as a selective inhibitor.
>
> Cheshire *et al.* discloses certain of phenoxypropylamines including Compound A as inhibitors of nitric oxide synthase. However, Cheshire *et al.* makes no teaching as to which compounds may or may not be selective nor does it teach the desirability of selective compounds which lack eNOS activity. Thus, a skilled artisan seeking to make alternate compounds that are inhibitors of nitric oxide synthase would choose a lead molecule which lacks undesirable eNOS activity and not Compound A which is disclosed as a general inhibitor of nitric acid synthase.

Applicant's remarks have been considered, however, they are not found to be persuasive. The prior art compound has desirable pharmacological activity, thus would be a candidate for further modification, regardless of alternate activity or lack thereof.

> These dramatic effects demonstrate the unpredictably of positional isomer changes in the medicinal chemistry of nitric oxide synthase inhibitors. Thus, a skilled artisan seeking to make alternate compounds that are inhibitors of nitric oxide synthase would not have a reasonable expectation that making a positional isomer of Compound A disclosed in Cheshire *et al.* would lead to an inhibitor of nitric oxide synthase.

The reference cited by the Applicant does not specifically apply to the compounds disclosed by Cheshire et al. It is maintained that positional isomers are of close structure. Thus, one of ordinary skill would have reasonable expectation of making additional compounds via this structural modification that display the desired pharmacological activity.

Conclusion

2. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Sun Jae Y. Loewe/
10-23-2009

/Golam M. M. Shameem/
Primary Examiner, Art Unit 1626